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☐ 1: Cancer Res. 1995 Dec 1;55(23):5548-50.

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Microsatellite instability and mutations of the transforming growth factor beta type II receptor gene in colorectal cancer.

Parsons R, Myeroff LL, Liu B, Willson JK, Markowitz SD, Kinzler KW, Vogelstein B.

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Johns Hopkins Oncology Center, Baltimore, Maryland 21231, USA.

The TGF beta type II receptor (RII) was found to be mutated within a polyadenine tract in 100 of 111 (90%) colorectal cancers with microsatellite instability. Other polyadenine tracts of similar length were mutated in these samples but not as frequently as RII. In most cases, the polyadenine tract mutations affected both alleles of RII, and in four tumors heterozygous for the polyadenine mutations, three had additional mutations that were expected to inactivate the other RII allele. These genetic data support the idea that RII behaves like a tumor suppressor during CR cancer development and is a critical target of inactivation in mismatch repair-deficient tumors.

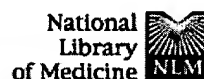
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Gastroenterology

Transforming growth factor beta type II receptor gene mutations in adenomas from hereditary nonpolyposis colorectal cancer.

Akiyama Y, Iwanaga R, Saitoh K, Shiba K, Ushio K, Ikeda E, Iwama T, Nomizu T, Yuasa Y.

Department of Hygiene and Oncology, School of Medicine, Tokyo Medical and Dental University, Japan.

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BACKGROUND & AIMS: Germline mutations of DNA mismatch repair genes are responsible for cancer susceptibility in hereditary nonpolyposis colorectal cancer (HNPCC) kindreds. Transforming growth factor beta type II receptor (TGF-beta RII) has been found to be somatically altered in HNPCC. The aim of this study was to clarify further the role of TGF-beta RII alterations in HNPCC tumorigenesis, particularly in adenomas. **METHODS:** Fourteen adenoma specimens and 13 cancer specimens from 10 patients with HNPCC were screened for mutations in the short repeated sequences of the TGF-beta RII gene by polymerase chain reaction-single-strand conformation polymorphism. Mismatch repair genes, replication errors, and c-K-ras 2 were also analyzed in HNPCC tumors. **RESULTS:** Alterations of the TGF-beta RII gene at the short poly(A) repeat were found in 8 (57%) adenoma specimens and 11 (85%) cancer specimens. They were found at an earlier stage of adenomas. Two adenoma specimens showed two-hit inactivation of mismatch repair genes. Replication errors were detectable in 13 (93%) adenoma specimens. Mutations in c-K-ras 2 codon 12 were detected at a 50% frequency in adenoma specimens. **CONCLUSIONS:** These data indicate a strong association between TGF-beta RII gene alterations and adenoma-carcinoma progression in HNPCC.

PMID: 8978340 [PubMed - indexed for MEDLINE]

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